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A case of dual chloroquine and halofantrine treatment failure in Zimbabwe

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SUMMARY

A case of malaria treatment failure with chloroquine and halofantrine is reported. The likely determinants and policy considerations are addressed.

INTRODUCTION

Global escalation of *Plasmodium falciparum* drug resistance continues to complicate treatment and pose a major setback for malaria control.[1-4] Resistance to chloroquine, the erstwhile most effective and safe drug, has spread to all but a few isolated foci over the past few decades.[1,4] This has seen the recent development and gradual introduction of novel and alternative antimalarial compounds such as artemisinine and its derivatives, and the phenathrene methanol halofantrine.

Chloroquine still remains the drug of first choice for treatment of uncomplicated malaria in Zimbabwe.

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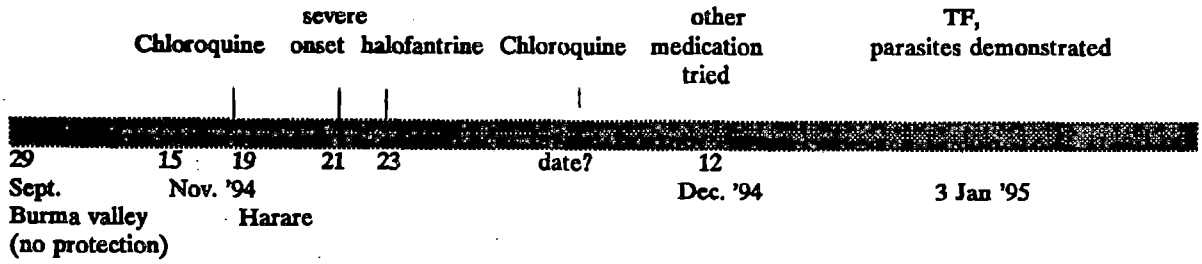
Figure I: Schedule of events pre and post treatment (TF, thick film).



resistant infections, and paucity of a streamlined service mechanism to perform sensitivity tests on suspected resistant cases, a few drugs have found their way into the market and often into prescription before local clinical evaluation. The present case report shows how this may be adding new dimensions to the malaria problem.

CASE REPORT

An adult male resident of Harare contracted malaria while working in an endemic irrigated commercial farm area of Mutare district (Burma Valley, ref 32° 48'E, 18° 35'S), from 27 September to 15 November 1994. The patient, who was not on prophylactic, suffered a clinical onset upon return to Harare and took a full adult course of chloroquine on 19 November 1994 (Figure I).

Owing to continuing illness despite treatment, on 23 November 1994 he saw a general practitioner and received a prescription of halofantrine (Halfan®), ie a total of six tablets of 250mg halofantrine hydrochloride, taken two six hourly. Clinical improvement even after the halofantrine course was only transient, however, and because of persisting symptoms a further course of chloroquine was taken (date unknown), which was not completed (a total of eight tablets of 150mg chloroquine base were taken), and subsequently, on 12 December, he revisited the GP. After protracted clinical episodes, amelliorated with analgesics (mostly paracetamol), on 3 January 1995 a thick film taken at Blair Research Laboratory was positive for *Plasmodium falciparum,* with >2 000 asexual parasites/µl blood prominent gametocytaemia. The patient was successfully cured with the sulfadoxine/pyrimethamine combination (Fansidar®, given as three tablets start of 1 500 mg sulfadoxine + 25mg pyrimethamine).

DISCUSSION

Because the patient was not cured prior to sulfadoxine/pyrimethamine treatment, and did not revisit a malaria endemic area, this case exhibited dual treatment failure to chloroquine and halofantrine. Most probably, the infection was chloroquine-resistant, which is hardly surprising as numerous cases have been documented in various parts of the country.[5-8] With halofantrine, however, failure to cure was likely due to malabsorption. Halofantrine is an effective antimalarial compound with no evidence of cross resistance to chloroquine.[2,9-10] Moreover, there has not been resistance selection pressure for the phenanthrene methanol, which is new in the country. It is known, though, that current tablet formulations of this sparingly soluble drug have shown evidence of erratic bioavailability in different individuals,[11] which has been related to treatment failure.[12-14] WHO recommended that better formulations of the drug be developed,[2] and indeed studies have recently been initiated on a new micronized formulation.[14-15]

In view of this potential intersubject variation in bioavailability it is recommended that local efficacy studies be conducted, with special emphasis on *in vivo* cure rates and bioabsorption. If malabsorption rates are substantial with wider introduction of the drug, prevalent subtherapeutic levels may select for halofantrine resistance and may not justify the relative cost of the drug. With the advent of drug resistance there is greater need for adherence to a rational drug policy tailored to the epidemiological situation and to minimising spread of drug resistance. The sending of heparinized blood specimens from suspect drug resistant cases to a central laboratory (eg Blair Research Laboratory) for *in vitro* confirmation needs to be strengthened. It may also be a beneficial alternative or complement to review such cases on day seven (and where possible day 14) post treatment,[16-17] whence thick film positivity would indi-

cate second line therapy, which in Zimbabwe is sulfadoxine/pyrimethamine.

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